

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of:

Hong LI, et al..

Appl. No.: Unassigned

Filed: October 27, 2003

For: ADENOVIRUS-MEDIATED  
INTRATUMORAL DELIVERY  
OF AN ANGIOGENESIS  
ANTAGONIST FOR THE  
TREATMENT OF TUMORS

Art Unit: Unassigned

Examiner: Unassigned

**Commissioner for Patents**  
Alexandria, VA 22313-1450

**INFORMATION DISCLOSURE STATEMENT**

Dear Sir:

Applicants submit copies of the PTO-1449 and PTO-892 referenced in parent application U.S. Serial No. 09/403,736 filed June 29, 2000, now allowed, for consideration and request that the U.S. Patent and Trademark Office make them of record in this application.

Applicants state the following:

☒ Each item of information contained in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the Information Disclosure Statement; or

☐ No item of information contained in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application, and to the knowledge of Applicant(s) no item of information contained in this Information Disclosure Statement was known to any individual designated in § 1.56(c) more than three months prior to the filing of this Information Disclosure Statement.

☐ In accordance with 37 C.F.R. § 1.97(b), this Information Disclosure Statement is believed to be submitted prior to issuance of a first Office Action and/or within three months of the filing date of the application. It is respectfully submitted that no fee is required for consideration of this information. However, in the event any fee is deemed necessary, the Commissioner is authorized to charge the undersigned's Deposit Account No. 50-1129.

☐ This Information Disclosure Statement is being submitted after the mailing of a non-final Office Action, but is believed to be prior to a final Office Action or a Notice of Allowance. Pursuant to 37 C.F.R. § 1.97(c), payment in the amount of \$180.00 as set forth in 37 C.F.R. § 1.17(p) is enclosed. The Commissioner is hereby authorized to charge any deficiency in the fees or charge any fee required to keep this application pending to our Deposit Account No. 50-1129.

While the information and references disclosed in this Information Disclosure Statement are submitted pursuant to 37 C.F.R. § 1.56, this submission is not intended to constitute an admission that any patent, publication or other information referred to is "prior art" to this invention. Applicants reserve the right to contest the "prior art" status of any information submitted or asserted against the application.

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material


PATENT  
Serial No. Unassigned  
Attorney Docket No.: A2778B

information as defined in 37 C.F.R. § 1.56(a) exists. This Information Disclosure Statement is in compliance with 37 C.F.R. § 1.98 and the Examiner is respectfully requested to consider the listed documents and information.

Dated: October 27, 2003

Respectfully submitted,  
**WILEY REIN & FIELDING LLP**

By:

  
David J. Kulik Reg. No. 36,576

**WILEY REIN & FIELDING LLP**  
Attn: Patent Administration  
1776 K Street, N.W.  
Washington, D.C. 20006  
**Telephone: 202.719.7000**  
**Facsimile: 202.719.7049**

# **Notice of References Cited**

Application/Control No.

09/403,736

Examiner

Eleanor Sorbello

Applicant(s)/Patent Under Reexamination  
LI ET AL.

Art Unit

1633

Page 1 of 1

## **U.S. PATENT DOCUMENTS**

*		DOCUMENT NO.	DATE	NAME	CLASS	SUBCLASS	DOCUMENT SOURCE **	
							APS	OTHER
<input type="checkbox"/>	A	6,080,728	Jun. 2000	Mixson	514	44	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	B						<input type="checkbox"/>	<input type="checkbox"/>
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## **FOREIGN PATENT DOCUMENTS**

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<input type="checkbox"/>	T							<input type="checkbox"/>	<input type="checkbox"/>

## **NON-PATENT DOCUMENTS**

*		DOCUMENT (Including Author, Title Date, Source, and Pertinent Pages)	DOCUMENT SOURCE **	
			APS	OTHER
<input type="checkbox"/>	U	Dang et al. Gene Therapy and Translational Cancer Therapy, Clinical Cancer Research, Vol 5, 471-474, Feb 1999	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	V	Eck, S.L. et al., 1996, Ch. 5. Gene Based Therapy, Goodman & Gillman's The Pharmacological basis of Therapeutics. page 77-101ck, et al.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	W	Robbins, Review: Viral Vectors for gene therapy, Trends in Biotechnology, Vol. 16, pages 35-40	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	X		<input type="checkbox"/>	<input type="checkbox"/>

\*A copy of this reference is not being furnished with this Office action. (See Manual of Patent Examining Procedure, Section 707.05(a).)

\*\*APS encompasses any electronic search i.e. text, image, and Commercial Databases.

J.S. Patent and Trademark Office

PTO-892 (Rev. 03-98)

Notice of References Cited

Part of Paper No. 9

# **Notice of References Cited**

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Reexamination  
LI ET AL.

Examiner

Eleanor Sorbello

Art Unit

1633

Page 1 of 1

## **U.S. PATENT DOCUMENTS**

*		Document Number	Date	Name	Classification	
		Country Code-Number-Kind Code	MM-YYYY			
	A	US-6,251,433	06-2001	Zuckermann et al	424	486
	B	US-5,652,095	07-1997	Taniguchi et al	435	6
	C	US-				
	D	US-				
	E	US-				
	F	US-				
	G	US-				
	H	US-				
	I	US-				
	J	US-				
	K	US-				
	L	US-				
	M	US-				

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*		Document Number	Date	Country	Name	Classification	
		Country Code-Number-Kind Code	MM-YYYY				
	N						
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	P						
	Q						
	R						
	S						
	T						

## **NON-PATENT DOCUMENTS**

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	Wilson, Vehicles for gene therapy, 1993, NAUTRE, Vol. 365, pp. 691-692
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	W	
	X	

\*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)  
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

# **Notice of References Cited**

Application/Control No.  
09/403,736

Applicant(s)/Patent Under Reexam  
Li et al.

Examiner  
Scott D. Priebe, Ph.D.

Art Unit  
1632

Page 1 of 1

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* A	Document Number Country Code-Number-Kind Code	Date MM-YYYY <sup>1</sup>	Name	Classification <sup>2</sup>	
	6,143,290	11/2000	Zhang et al.	424	93.2
	5,885,795	3/1999	O'Reilly et al.	435	69.1

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* N	Document Number Country Code-Number-Kind Code	Date MM-YYYY <sup>1</sup>	Country	Name	Classification <sup>2</sup>	

## **NON-PATENT DOCUMENTS**

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		Tanaka et al., "Viral vector-mediated transduction of modified platelet factor 4 cDNA inhibits angiogenesis and tumor growth," Nature Med. 3 (4): 437-442, April 5, 1997.
	V	Tanaka et al., "Retroviral and adenoviral mediated transduction of angiostatin cDNA inhibits angiogenesis and tumor growth," Proc. Amer. Assoc. Cancer Res. 38: 264, March 1997.
	W	
	X	

A copy of this reference is not being furnished with this Office action. See MPEP § 707.05(a).

<sup>1</sup> Dates in MM-YYYY format are publication dates.

<sup>2</sup> Classifications may be U.S. or foreign.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(use as many sheets as necessary)</i>				<b>Complete if Known</b>	
				Application No.	09/403,736
				Filing Date	10/26/1999
				Group Art Unit	1632
				Examiner Name	S. Priebe
Sheet	1	Of	1	Attorney Docket No.	A2778A-US
<b>U.S. PATENT DOCUMENTS</b>					
Examiner Initials*	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document		Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
<b>FOREIGN PATENT DOCUMENTS</b>					
Examiner Initials*	Country Code	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant in Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
<b>OTHER PRIOR ART—NON PATENT LITERATURE DOCUMENTS</b>					
Examiner Initials*	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page (s), volume-issue number(s), publisher, city and/or country where published				T <sup>1</sup>
	Abstract #1171 of an article by FUJIWARA et al., titled "Antiangiogenic therapy for human lung cancer by wild-type p53-mediated downregulation of vascular endothelial growth factor (VEGF) expression," Pharmacology/Therapeutics (Preclinical and Clinical) 12, p. 175.				
Examiner Signature				Date Considered	

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>Applicant is to place a check mark here if English language Translation is attached.

FORM PTO-1449 (Modified) (REV. 7-80)	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO.	APPLICATION NO.
LIST OF REFERENCES CITED BY APPLICANT  (Use several sheets if necessary)		A2778A-US	09/403,736
		APPLICANT	
		Hong LI <i>et al.</i>	
		FILING DATE	GROUP
		October 26, 1999	1633

## U.S. PATENT DOCUMENTS

*EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

## FOREIGN PATENT DOCUMENTS

DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION
					YES NO

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)

	Palmer, Gyorffy, <i>et al.</i> "Combined treatment of a murine breast cancer model with type 5 adenovirus vectors expressing murine angiostatin and il-12: a role for combined anit-angiogenesis and immunotherapy," <i>J. Immunol.</i> , May 15, 2001, 166(10):6212-7. (Abstract only)
	Pili, R., <i>et al.</i> "Adenovirus-mediated gene transfer of fibroblast growth factor-1: angiogenesis and tumorigenicity in nude mice," <i>Int. J. Cancer</i> , Oct. 9, 1997, 73(2):258-63. (Abstract only)
	Matsumoto, G., <i>et al.</i> "Angiostatin gene therapy inhibits the growth of murine squamous cell carcinoma in vivo," <i>Oral Oncol</i> , June 2001, 37(4):369-78. (Abstract only)
	Riccioni, T., <i>et al.</i> "Adenovirus-mediated wild-type p53 overexpression inhibits endothelial cell differentiation in vitro and angiogenesis in vivo," <i>Gene Ther</i> , June 1998, 5(6):747-54. (Abstract only)

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\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include a copy of this form with next communication to applicant.



ATTY. DOCKET NO.

APPLICATION NO.

A2778A-US

09/403,736

### LIST OF REFERENCES CITED BY APPLICANT

(Use several sheets if necessary)

APPLICANT

Hong LI *et al.*

FILING DATE

October 26, 1999

GROUP

1633

## U.S. PATENT DOCUMENTS

[illegible]

## FOREIGN PATENT DOCUMENTS

[illegible]

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)**

		GenBank entry for human plasminogen and annotations from NCBI web page
		GenBank entry for human urokinase-type plasminogen activator and annotations from NCBI

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Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

1449A/PTO		U.S. Department of Commerce Patent and Trademark Office		Complete if Known	
<b>LIST OF PRIOR ART CITED BY APPLICANT</b> <i>(use as many sheets as necessary)</i>				Application Number	09/403,736
				Filing Date	26 October 1999
				First Named Inventor	Li et al.
				Group Art Unit	
				Examiner Name	
Sheet	1	of	19	Attorney Docket Number	A2778A-US

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Examiner Initials	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code (if known)			
	AA	4,650,764		Temin et al.	03-17-1987	
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		Office	Number	Kind Code (if known)				
	FA	EP	185 573		Perricaudet et al.	06-25-1986		
	FB	EP	253 738		Colin et al.	07-17-1986		
	FC	WO	89/07150		Bank et al.	08-10-1989		
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	FH	WO	91/17976		Correa et al.	11-28-1991		
	FI	EP	178 220		Jacob et al.	02-01-1992		

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Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

1449A/PTO		U.S. Department of Commerce Patent and Trademark Office		Complete if Known	
<b>LIST OF PRIOR ART CITED BY APPLICANT</b> <i>(use as many sheets as necessary)</i>				Application Number	09/403,736
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				Group Art Unit	
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Sheet	2	of	19	Attorney Docket Number	A2778A-US

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Examiner Initials	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code (if known)			
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	AM	5,385,839		Stinski	01-31-1995	
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Examiner Initials	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T
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	FJ	WO	92/05263		Inglis et al.	04-02-1992		
	FK	WO	93/00928		Bastarty et al.	01-21-1993		
	FL	WO	93/00929		Bastart et al.	01-21-1993		
	FM	WO	93/09239		Srivastava	05-13-1993		
	FN	WO	93/15199		Fleer et al.	08-05-1993		
	FO	WO	94/12649		Gregory et al.	06-09-1994		
	FP	WO	94/21807		Inglis et al.	09-29-1994		
	FQ	WO	94/26914		Haddada et al.	11-24-1994		
	FR	WO	94/28152		Imler et al.	12-08-1994		

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## LIST OF PRIOR ART CITED BY APPLICANT

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Application Number	09/403,736
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Group Art Unit	
Examiner Name	
Attorney Docket Number	A2778 A-US

Sheet	3	of	19
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## U.S. PATENT DOCUMENTS

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## FOREIGN PATENT DOCUMENTS

Examiner initials	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T
		Office	Number	Kind Code (if known)				
	FS	WO	94/28938		Wilson et al.	12-22-1994		
	FT	WO	95/02697		Perricaudet et al.	01-26-1995		
	FU	WO	95/07358		Dougherty et al.	03-16-1995		
	FV	WO	95/18863		Behr et al.	07-13-1995		
	FW	WO	95/21931		Bazile et al.	08-17-1995		
	FX	WO	95/28494		Overell et al.	10-26-1995		
	FY	WO	95/29242		O'Reilly et al.	11-02-1995		
	FZ	EP	488 528		Lebkowski et al.	11-29-1995		
	GA	WO	96/01313		Bujard et al.	01-18-1996		

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		Office	Number	Kind Code (if known)				
	GB	WO	96/01815		Authelin et al.	01-25-1996		
	GC	FR	2726285		Yeh et al.	05-03-1996		
	GD	WO	96/17823		Byk et al.	06-13-1996		
	GE	WO	96/22378		Dedieu et al.	07-25-1996		
	GF	WO	96/25508		Byk et al.	08-22-1996		
	GG	WO	97/04092		Conseiller et al.	02-06-1997		
	GH	WO	97/15666		O'Reilly et al.	05-01-1997		

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				Examiner Name	
Sheet	5	of	19	Attorney Docket Number	A2778 A-US

## OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, country, where published, source.	T
	PA	Estreicher et al., The Receptor for Urokinase Type Plasminogen Activator Polarizes Expression of the Protease to the Leading Edge of Migrating Monocytes and Promotes Degradation of Enzyme Inhibitor Complexes, Journal of Cell Biology 111, 783-792 (1990)	
	PB	Pepper et al., Chondrocytes Inhibit Endothelial Sprout Formation In Vitro: Evidence for Involvement of a Transforming Growth Factor-Beta, Journal of Cellular Physiology 146, 170-179 (1991)	
	PC	Ploug et al., Cellular Receptor for Urokinase Plasminogen Activator, The Journal of Biological Chemistry 266(3), 1926-1933 (1991)	
	PD	Ellis et al., Plasminogen Activation by Receptor-bound Urokinase, The Journal of Biological Chemistry 266(19), 12752-12758 (1991)	
	PE	Wei et al., Identification of the Urokinase Receptor as an Adhesion Receptor for Vitronectin, The Journal of Biological Chemistry 269(51), 32380-32388 (1994)	
	PF	Appella et al., The Receptor-binding Sequence of Urokinase: A Biological Function for the Growth-Factor Module of Proteases, The Journal of Biological Chemistry 262(10), 4437-4440 (1987)	
	PG	Cao et al., Kringle Domains of Human Angiostatin, The Journal of Biological Chemistry 271(46), 29461-29467 (1996)	
	PH	Imren et al., Overexpression of Tissue Inhibitor of Metalloproteinases-2 by Retroviral-mediated Gene Transfer in Vivo Inhibits Tumor Growth and Invasion, Cancer Research 56, 2891-2895 (1996)	

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Application Number	09/403,736
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First Named Inventor	Li et al.
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	PI	Shapiro et al., Induction of Primary Cutaneous Melanocytic Neoplasms in Urokinase-Type Plasminogen Activator (uPA)-deficient and Wild-Type Mice: Cellular Blue Nevi Invade but Do Not Progress to Malignant Melanoma in uPA-deficient Animals, Cancer Research 56, 3597-3604 (1996)	
	PJ	Skladanowski et al., Expression of Wild-Type p53 Increases Etoposide Cytotoxicity in M1 Myeloid Leukemia Cells by Facilitated G2 to M Transition: Implication for Gene Therapy, Cancer Research 57, 818-823 (1997)	
	PK	Sim et al., A Recombinant Human Angiostatin Protein Inhibits Experimental Primary and Metastatic Cancer, Cancer Research 57, 1329-1334 (1997)	
	PL	Liotta et al., Quantitative Relationships of Intravascular Tumor Cells, Tumor Vessels, and Pulmonary Metastases following Tumor Implantation, Cancer Research 34, 997-1004 (1974)	
	PM	Hori et al., Suppression of Solid Tumor Growth by Immunoneutralizing Monoclonal Antibodies against Human Basic Fibroblast Growth Factor, Cancer Research 51, 6180-6184 (1991)	
	PN	Min et al., Urokinase Receptor Antagonists Inhibit Angiogenesis and Primary Tumor in Syngeneic Mice, Cancer Research 56, 2428-2433 (1996)	
	PO	Wei et al., Regulation of Integrin Function by the Urokinase Receptor, Science 273, 1551-1555 (1996)	
	PP	Graeber et al., Hypoxia-mediated selection of cells with diminished apoptotic potential in solid tumours, Nature 379, 88-91 (1996)	

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	PQ	Bacharach et al., In vivo patterns of expression of urokinase and its inhibitor PAI-1 suggest a concerted role in regulating physiological angiogenesis, Cell Biology 89, 2632-2636 (1989)	
	PR	He et al., Tissue cooperation in a proteolytic cascade activating human interstitial collagenase, Proc. Natl. Acad. Sci. 86, 2632-2636 (1989)	
	PS	Crowley et al., Prevention of metastasis by inhibition of the urokinase receptor, Proc. Natl. Acad. Sci. 90, 5021-5025 (1993)	
	PT	Davis et al., Monoclonal antibodies to mitotic cells, Proc. Natl. Acad. Sci. 80, 2926-2930 (1983)	
	PU	Gupta et al., A potent inhibitor of endothelial cell proliferation is generated by proteolytic cleavage of the chemokine platelet factor 4, Proc. Natl. Acad. Sci. 92, 7799-7803 (1995)	
	PV	Mignatti et al., Biology & Biochemistry of Proteinases in Tumor Invasion, Physiological Reviews 73(1), 161-195 (1993)	
	PW	Pyke et al., Urokinase-type Plasminogen Activator is Expressed in Stromal Cells and Its Receptor in Cancer Cells and Its Receptor in Cancer Cells at Invasive Foci in Human Colon Adenocarcinomas, American Journal of Pathology 138(5), 1059-1067 (1991)	
	PX	Magdolen et al., Systematic mutational analysis of the receptor-binding region of the human urokinase-type plasminogen activator, Eur J. Biochem 237, 743-751 (1996)	

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	PY	Schmitt et al., Tumor-associated Proteases, Fibrinolysis 6(4), 3-26 (1992)	
	PZ	Stratford-Perricaude et al., Widespread Long-term Gene Transfer to Mouse Skeletal Muscles and Heart, J. Clin. Invest. 90, 626-630 (1992)	
	QA	Weidner et al., Tumor Angiogenesis and Metastasis-Correlation in Invasive Breast Carcinoma; The New England Journal of Medicine 324(1), 1-8 (1991)	
	QB	Hanahan et al., Patterns and Emerging Mechanisms of the Angiogenic Switch during Tumorigenesis, Cell 86, 353-364 (1996)	
	QC	Wickham et al., Integrins avB3 and avB5 Promote Adenovirus Internalization but Not Virus Attachment, Cell 73, 309-319 (1993)	
	QD	Brooks et al., Integrin avB3 Antagonists Promote Tumor Regression by Inducing Apoptosis of Angiogenic Blood Vessels, Cell 79, 1157-1164 (1994)	
	QE	O'Reilly et al., Endostatin: An Endogenous Inhibitor of Angiogenesis and Tumor Growth, Cell 88, 277-285 (1997)	
	QF	Dong et al., Macrophage-Derived Metalloelastase Is Responsible for the Generation of Angiostatin in Lewis Lung Carcinoma, Cell 88, 801-810 (1997)	

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	QG	King et al., Mitosis in Transition, Cell 79, 563-571 (1994)	
	QH	Yeh et al., Advances in adenoviral vectors: from genetic engineering to their biology, FASEB 11, 615-623 (1997)	
	QI	Folkman, What Is the Evidence That Tumors Are Angiogenesis Dependent?, Journal of the National Cancer Institute 82(1), 4-6 (1990)	
	QJ	Mirshahi et al., Evaluation of the Inhibition by Heparin and Hirudin of Coagulation Activation During r-tPA-Induced Thrombolysis, Blood, 74(3) 1025-1030 (1989)	
	QK	Plate et al., Vascular endothelial growth factor is a potential tumour angiogenesis factor in human gliomas in vivo, Nature 359, 845-848 (1992)	
	QL	Roth et al., Gene Therapy for Cancer: What Have We Done and Where Are We Going?, Journal of the National Cancer Institute 89(1), 21-39 (1997)	
	QM	Clapp et al., The 16-Kilodalton N-Terminal Fragment of Human Prolactin Is a Potent Inhibitor of Angiogenesis, Endocrinology 133(3), 1292-1299 (1993)	
	QN	Kim et al., Inhibition of vascular endothelial growth factor-induced angiogenesis suppresses tumour growth in vivo, Nature 362, 841-844 (1993)	

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	QO	Hamada et al., Separable growth and migration factors for large-cell lymphoma cells secreted by microvascular endothelial cells derived from target organs for metastasis, Br. J. Cancer 66, 349-354 (1992)	
	QP	Trochon et al., Evidence of Involvement of CD44 In Endothelial Cell Proliferation, Migration and Angiogenesis In Vivo, Int. J. Cancer 66, 664-668 (1996)	
	QQ	Fan et al., Controlling the vasculature: angiogenesis, anti-angiogenesis and vascular targeting of gene therapy, TIPS 16, 57-66 (1995)	
	QR	Rifkin et al., Growth factor control of extracellular proteolysis, Cell Differentiation & Development 32, 313-318 (1990)	
	QS	Lu et al., Blockage of urokinase receptor reduces in vitro the motility and the deformability of endothelial cells, FEBS Letters 380, 21-24 (1996)	
	QT	Kobayashi et al., Inhibition of Metastasis Of Lewis Lung Carcinoma By A Synthetic Peptide Within Grown Factor-Like Domain Of Urokinase In The Experimental and Spontaneous Metastasis Model, Int. J. Cancer 57, 727-733 (1994)	
	QU	Lu et al., Blockage of the urokinase receptor on the cell surface: construction and characterization of a hybrid protein consisting of the N-terminal fragment of human urokinase and human albumin, FEBS Letters 356, 56-59 (1994)	
	QV	Holmgren et al., Dormancy of micrometastases: Balanced proliferation and apoptosis in the presence of angiogenesis suppression, Nature Medicine 1(2), 149-153 (1995)	

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	QW	Graham et al., Characteristics of a Human Cell Line Transformed by DNA from Human Adenovirus Type 5, J. Gen. Virol. 36, 59-72 (1977)	
	QX	Hayes et al., Carbohydrate of the Human Plasminogen Variants, The Journal of Biological Chemistry 254(18), 8772-8776 (1979)	
	QY	Roldan et al., Cloning and expression of the receptor for human urokinase plasminogen activator, a central molecule in cell surface, plasmin dependent proteolysis, The EMBO Journal 9(2), 467-474 (1990)	
	QZ	Hirt, Selective Extraction of Polyoma DNA from Infected Mouse Cell Cultures, J. Mol. Biol. 26, 365-369 (1967)	
	RA	Folkman, Angiogenesis in cancer, vascular, rheumatoid and other disease, Nature Medicine 1(1), 27-31 (1995)	
	RB	Belin et al., Cloning, nucleotide sequencing and expression of cDNAs encoding mouse urokinase-type plasminogen activator, Eur. J. Biochem 148, 225-232 (1985)	
	RC	Naldini et al., Extracellular proteolytic cleavage by urokinase is required for activation of hepatocyte growth factor/scatter factor, The EMBO Journal 11(13), 4825-4833 (1992)	
	RD	O'Reilly et al., Angiostatin induces and sustains dormancy of human primary tumors in mice, Nature Medicine 2(6), 689-692 (1996)	

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	RM	Markowitz et al., A Safe Packaging Line for Gene Transfer: Separating Viral Genes on Two Different Plasmids, Journal of Virology 62(4), 1120-1124 (1988)	
	RN	Kuo et al., Efficient Gene Transfer Into Primary Murine Lymphocytes Obviating the Need for Drug Selection, Blood 82(3), 845-852 (1993)	
	RO	Machy et al., Gene transfer from targeted liposomes to specific lymphoid cells by electroporation, Proc. Natl. Acad. Sci. 85, 8027-8031 (1988)	
	RP	Felgner et al., Lipofection: A highly efficient, lipid-mediated DNA-transfection procedure, Proc. Natl. Acad. Sci. 84, 7413-7417 (1987)	
	RQ	Bender et al., Evidence that the Packaging Signal of Moloney Murine Leukemia Virus Extends into the gag Region, Journal of Virology 1639-1646 (1987)	
	RR	Ulmer et al., Heterologous Protection Against Influenza by Injection of DNA Encoding a Viral Protein, Scienc 259, 1745-1749 (1993)	
	RS	Le Gal La Salle et al., An Adenovirus Vector For Gene Transfer into Neurons and Glia in the Brain, Science 259, 988-990 (1993)	
	RT	Samulski et al., A Recombinant Plasmid from Which an Infectious Adeno-Associated Virus Genome Can Be Excised In Vitro and Its use To Study Viral Replication, Journal of Virology 61(10), 3096-3101 (1987)	

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	RE	Dvorak et al., Identification and Characterization of the Blood Vessels of Solid Tumors That Are Leaky to Circulating Macromolecules, American Journal of Pathology 133(1), 95-109 (1988)	
	RF	Readhead et al., Expression of a Myelin Basic Protein Gene in Transgenic Shiverer Mice: Correction of the Dysmyelinating Phenotype, Cell, 48, 703-712 (1987)	
	RG	Kollias et al., Regulated Expression of Human A Gamma, Beta, and Hybrid Gamma Beta-Globin Genes in Transgenic Mice: Manipulation of the Developmental Expression Patterns, Cell 46, 89-94, (1986)	
	RH	Leder et al., Consequences of Widespread Deregulation of the c-myc Gene in Transgenic Mice: Multiple Neoplasms and Normal Development, Cell 45, 485-495 (1986)	
	RI	Yamamoto et al., Identification of a Functional Promoter in the Long Terminal Repeat of Rous Sarcoma Virus, Cell 22, 787-797 (1980)	
	RJ	Mann et al., Construction of a Retrovirus Packaging Mutant and Its Use to Produce Helper-Free Defective Retrovirus, Cell 33, 153-159 (1983)	
	RK	Swift et al., Tissue-Specific Expression of the Rat Pancreatic Elastase I Gene in Transgenic Mice, Cell 38, 639-646 (1984)	
	RL	Grosschedl et al., Introduction of a Micro Immunoglobulin Gene into the Mouse Germ Line: Specific Expression in Lymphoid Cells and Synthesis of Functional Antibody, Cell 38, 647-658 (1984)	

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	RM	Lebkowski et al., Adeno-Associated Virus: a Vector system for Efficient Introduction and Integration of DNA into a Variety of Mammalian Cell Types, Molecular & Cellular Biology 8(10), 3988-3996 (1988)	
	RN	Alexander et al., Expression of the c-myc Oncogene under Control of an Immunoglobulin Enhancer in Eu-myc Transgenic Mice, Molecular & Cellular Biology 7(4), 1436-1444 (1987)	
	RO	Krumlauf et al., Developmental Regulation of alpha-Fetoprotein Genes in Transgenic Mice, Molecular & Cellular Biology 5(7), 1639-1648 (1985)	
	RP	Hammer et al., Diversity of Alpha-Fetoprotein Gene Expression in Mice Is Generated by a Combination of Separate Enhancer Elements, Science 235, 53-58 (1987)	
	RQ	Mason et al., The Hypogonadal Mouse: Reproductive Functions Restored by Gene Therapy, Science 234, 1372-1378 (1986)	
	RR	Williams et al., Introduction of foreign genes into tissues of living mice by DNA-coated microprojectiles, Proc. Natl. Acad. Sci. 88, 2726-2730 (1991)	
	RS	DeBoer et al., The tac promoter: A functional hybrid derived from the trp and lac promoters, Proc. Natl. Acad. Sci. 80, 21-25 (1983)	
	RT	Villa-Komaroff et al., A bacterial clone synthesizing proinsulin, Proc. Natl. Acad. Sci. 75(8), 3727-3731 (1978)	

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	RU	Wagner et al., Nucleotide sequence of the thymidine kinase gene or herpes simplex virus type 1, Proc. Natl. Acad. Sci. 78(3), 1441-1445 (1981)	
	RV	Hutchison et al., A complete library of point substitution mutations in the glucocorticoid response element of mouse mammary tumor virus, Proc. Natl. Acad. Sci. 83, 710-714 (1986)	
	RW	Wu et al., Receptor-mediated Gene Delivery and Expression in Vivo, Journal of Biological Chemistry 263(29), 14621-14624 (1988)	
	RX	Wilson et al., Hepatocyte-directed Gene Transfer in Vivo Leads to Transient Improvement of Hypercholesterolemia in Low Density Lipoprotein Receptor-deficient Rabbits, Journal of Biological Chemistry 267(2), 963-967 (1992)	
	RY	Wu et al., Receptor-mediated in Vitro Gene Transformation by a Soluble DNA Carrier System, Journal of Biological Chemistry 262(10), 4429-4432 (1987)	
	RZ	Benoist et al., In vivo sequence requirements of the SV40 early promoter region, Nature 290, 304-310 (1981)	
	SA	Brinster et al., Regulation of metallothionein-thymidine kinase fusion plasmids injected into mouse eggs, Nature 296, 39-42 (1982)	
	SB	Shani, Tissue-specific expression of rat myosin light-chain 2 gene in transgenic mice, Nature 314, 283-286 (1985)	

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				Filing Date	26 October 1999
				First Named Inventor	Li et al.
				Group Art Unit	
				Examiner Name	
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## OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

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	SC	Hanahan, Heritable formation of pancreatic Beta-cell tumours in transgenic mice expressing recombinant insulin/simian virus 40 oncogenes, Nature 315, 115-122 (1985)	
	SD	Magram et al., Developmental regulation of a cloned adult Beta-globin gene in transgenic mice, Nature 315, 338-340 (1985)	
	SE	Gilbert et al., Useful Proteins from Recombinant Bacteria, Scientific American 242(4), 74-94 (1980)	
	SF	Kaplitt et al., Expression of a Functional Foreign Gene in Adult Mammalian Brain following in Vivo Transfer via a Herpes Simplex Virus Type 1 Defective Viral Vector, Molecular & Cellular Neurosciences 2, 320-330 (1991)	
	SG	Samulski et al., Helper-Free Stocks of Recombinant Adeno-Associated Viruses: Normal Integration Does Not Require Viral Gene Expression, Journal of Virology 63(9), 3822-3828 (1989)	
	SH	Beard et al., Transcription Mapping of Mouse Adenovirus Type 1 Early Region 3, Virology 175, 81-90 (1990)	
	SI	Levero et al., Defective and nondefective adenovirus vectors for expressing foreign genes in vitro and in vivo, Gene 101, 195-202 (1991)	
	SJ	Graham, Covalently closed circles of human adenovirus DNA are infectious, The EMBO Journal 3(12), 2917-2922 (1984)	

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	SK	Pinkert et al., An albumin enhancer located 10 kb upstream functions along with its promoter to direct efficient, liver-specific expression in transgenic mice, Genes & Development 1, 268-276 (1987)	
	SL	Adams et al., The c-myc oncogene driven by immunoglobulin enhancers induces lymphoid malignancy in transgenic mice, Nature 318, 533-538 (1985)	
	SM	Kelsey et al., Species- and tissue-specific expression of human alpha1-antitrypsin in transgenic mice, Genes & Development 1, 161-171 (1987)	
	SN	Johnson et al., Inhibition of Angiogenesis by Tissue Inhibitor of Metalloproteinase, Journal of Cellular Physiology 160, 194-202 (1994)	
	SO	Wilhelm et al., Recombinant soluble urokinase receptor as a scavenger for urokinase-type plasminogen activator (uPA) Inhibition of proliferation and invasion of human ovarian cancer cells, FEBS Letters 337, 131-134 (1994)	
	SP	Hutchinson et al., Mutagenesis at a Specific Position in a DNA Sequence, The Journal of Biological Chemistry 253(18), 6551-6560 (1978)	
	SQ	Oliphant et al., Cloning of random-sequence oligodeoxynucleotides, Gene 44, 177-183 (1986)	
	SR	Bernstein et al., Gene Transfer with Retrovirus Vectors, Genetic Engineering 7, 235-261 (1985)	

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	SS	McCormick, Human Gene Therapy: The First Round, Bio/Technology 3(8), 689-693 (1985)	
	ST	Miller et al., Improved Retroviral Vectors for Gene Transfer and Expression, BioTechniques 7(9), 980-990 (1989)	
	SU	Felgner et al., Cationic liposome-mediated transfection, Nature 337, 387-388 (1989)	
	SV	Curiel et al., High-Efficiency Gene Transfer Mediated by Adenovirus Coupled to DNA-Polylysine Complexes, Human Gene Therapy 3, 147-154 (1992)	
	SW	Zoller et al., Laboratory Methods -- Oligonucleotide-Directed Mutagenesis: A Simple Method Using Two Oligonucleotide Primers and a Single-Stranded DNA Template, DNA 3(6), 479-488 (1984)	
	SX	MacDonald, Expression of the Pancreatic Elastase I Gene in Transgenic Mice, Hepatology 7(1), 42S-51S (1987)	
	SY	O'Reilly et al., Angiostatin: A Novel Angiogenesis Inhibitor That Mediates the Suppression of Metastases by a Lewis Lung Carcinoma, Cell 79, 315-328 (1994)	
	SZ	Dedieu et al., Long-Term Gene Delivery into the Livers of Immunocompetent Mice with E1/E4-Defective Adenovirus, Journal of Virology 71(6), 4626-4637 (1997)	

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	TA	Mirshahi et al., A monoclonal antibody directed against an epitope in the NH2-terminal region of native human plasminogen induced a modification of its functional properties, Fibrinolysis & Proteolysis 11(3), 155-163 (1997)	
	TB	Farrell, Recombinant Herpesviruses Lacking Gene For Glycoprotein L, RD#37105A by Cantab Pharmaceuticals Res. Ltd (1995)	

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